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Protective Antibodies against Equine Encephalomyelitis Virus in the Serum of Laboratory Workers.

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It has been shown recently[1] that a large proportion of mice and guinea pigs develop, with increasing age, physiological or structural barriers that prevent certain viruses from invading the central nervous system. This resistance is demonstrable when virus is given peripherally, as, for example, intraäbdominally or intramuscularly, but not when it is injected directly into the brain. It is not a result of prior infection nor is it associated with the presence of protective

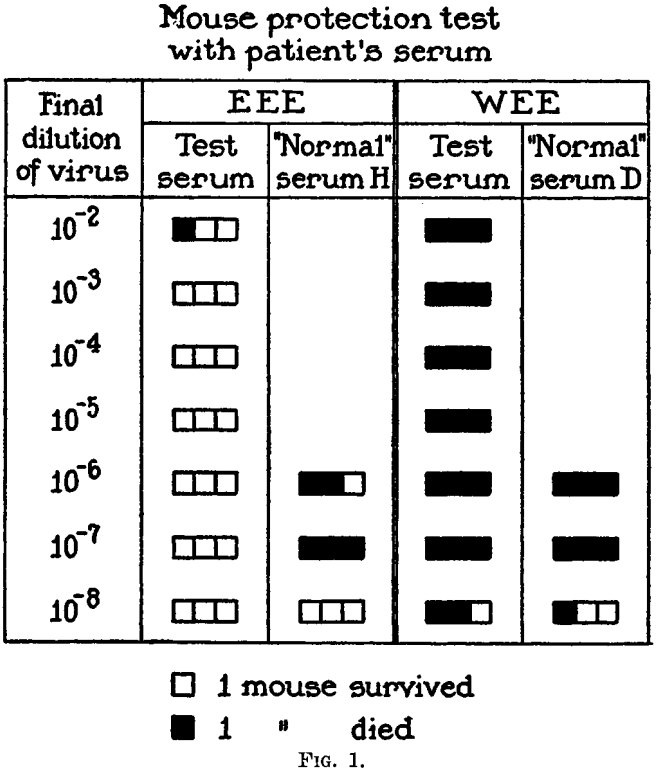

FIG. 1.

[1] Sabin, A. B., and Olitsky, P. K., *J. Exp. Med.*, 1937, **66**, 15, 35; 1938, **67**, 201, 229; Sabin, A. B., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 270; Sabin, A. B., and Olitsky, P. K., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 595, 597.

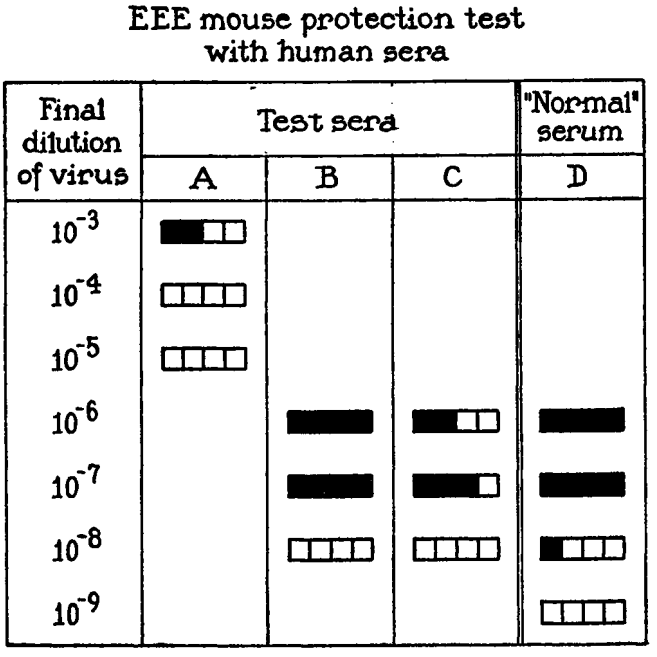

FIG. 2.

substance in the serum. Furthermore, in the recent epidemic of equine encephalomyelitis (E. E.) in man in southeastern Massachusetts,[2] children were predominantly affected. The older animals which resist the E. E. viruses develop systemic infection, as is evidenced by the finding of virus in the circulation and later the presence of protective antibodies in the serum. In view of this suggestive relationship of age of both the experimental animal and man to clinically apparent infection with this virus, it was thought desirable to undertake a study of the protective capacity of the serum in certain individuals in our laboratory, who had been in contact with the E. E. virus for a period extending from 1 to over 6 years. The results would indicate whether a clinically inapparent infection, as determined by the presence of protective antibody, could possibly have occurred during that time.

Serum-protection tests were carried out in mice by the intra-abdominal method of Olitsky and Harford;[3] that is, by injecting,

[2] Fothergill, L. D., Dingle, J. H., Farber, S., and Connerley, M. L., *New England J. Med.*, 1938, **219**, 411; Webster, L. T., and Wright, F. H., *Science*, 1938, **88**, 305; Feemster, R. F., *Am. J. Pub. Health*, 1938, **28**, 1403; Wesselhoeft, E., Smith, E. C., and Branch, C. F., *J. Am. Med. Assn.*, 1938, **111**, 1735.

[3] Olitsky, P. K., and Harford, C. G., *J. Exp. Med.*, 1938, **68**, 173.

by the intraäbdominal route, 0.03 cc of a mixture of equal parts of test serum and virus-dilutions (tenfold dilutions were used) into 15-day-old mice. Each mixture was given to groups of 3 or 4 mice. The Eastern strain of virus (E. E. E.) was derived from a stock which was frequently passaged in mouse brain and was again passaged through mouse brains immediately before use.

Two human sera, H and D, considered as "normal", were employed. The first was obtained from a worker in this laboratory in 1931 before the virus had been introduced here for study; the second was collected in January, 1938, and had been previously shown to afford no protection against E. E. E. virus. The titer of the virus in the control series, with or without these sera, was 10^{-7} or 10^{-8} (Figs. 1, 2, and 3). Another serum was added* which was obtained from a patient who 5 weeks previously had become acutely ill and had developed encephalomyelitis followed by recovery. This patient had been engaged in the procedure of inoculating E. E. virus in chick embryos. The serum, after the acute illness, protected mice against 100,000 minimal infective intraäbdominal doses of E. E. E. virus by the intraäbdominal test and showed no protection against the Western strain (W. E. E.) (Fig. 1).

Of the 6 sera collected from the individual members of our laboratory, 5 revealed no protective antibodies against E. E. E. virus (Figs. 2 and 3); variations are not significant, as shown by the con-

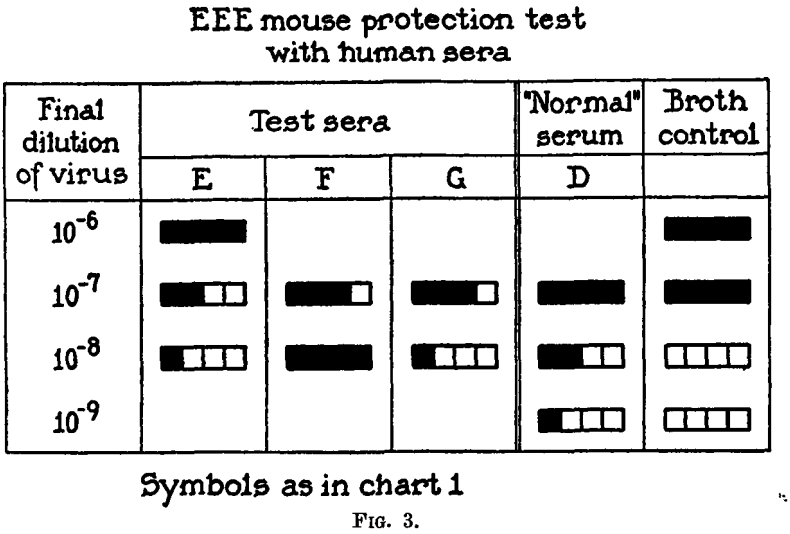

FIG. 3.

* We express with pleasure our deep obligation to Dr. J. H. Warvel of Indianapolis, Indiana, for this material and the history of the case.

trols. On the other hand, one (A) protected against 1,000 to 10,000 intraäbdominal lethal doses. The latter was obtained from a person who has been associated with work on E. E. virus (mostly the Eastern strain) for 6 years; at no time has he passed through an illness resembling encephalomyelitis and his general health has remained excellent. None of the 6 sera showed protective antibodies against the W. E. E. strain.

In view of the recently presented hypothesis that localized barriers develop with increasing age, or are present in particular hosts,[1] which prevent certain viruses from invading the CNS, the positive result herein reported of the presence of protective antibodies in an adult person who has been exposed to the virus in the laboratory, takes on added interest. A suggestion offered[4] is that in man, if the pattern of viral invasion from the periphery to the CNS follows that in the mouse or guinea pig, then the probability exists that in most human adults the virus may perhaps be prevented from invading the CNS by certain localized barriers. Hence adult contacts during an epidemic may have clinically inapparent infection and possibly reveal virus in the circulation. In such instances protective antibodies may be found later in the serum. Proof of this assumption would, of course, depend on further observations in the field.

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Metabolism of "Sulfapyridine-Fast" and Parent Strains of Pneumococcus Type I.

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The acquisition of "sulfapyridine-fastness" by a strain of Pneumococcus Type I has been described.[1] This induced "fastness" is associated with a fairly stable alteration in metabolism without changes in morphology, type-specificity, or virulence of the pneumococcus. The present communication deals with certain of the biochemical activities of the "drug-fast" and parent strains, together with observations concerning the action of sulfapyridine on the pneumococcus.

On the usual culture media, the drug-fast strain grows as well as the parent strain and ferments the same sugars.

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4 Sabin, A. B., personal communication.

1 MacLeod, C. M., and Daddi, G., PROC. SOC. EXP. BIOL. AND MED., in press.